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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/750,609	12/28/2000	David Robertson	1242/27/2/2	6747

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EXAMINER	
CHUNDURU, SURYAPRABHA	
ART UNIT	**PAPER NUMBER**
1637	

DATE MAILED: 04/13/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action Before the Filing of an Appeal Brief	**Application No.** 09/750,609	**Applicant(s)** ROBERTSON ET AL.	
	Examiner Suryaprabha Chunduru	**Art Unit** 1637	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 22 March 2005 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☐ The period for reply expires _____ months from the mailing date of the final rejection.
   b) ☒ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☒ The reply was filed after the date of filing a Notice of Appeal, but prior to the date of filing an appeal brief. The Notice of Appeal was filed on *22 March 2005*. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: *none*.
   Claim(s) objected to: *none*.
   Claim(s) rejected: *1-17 and 80*.
   Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08 or PTO-1449) Paper No(s). _____
13. ☐ Other: _____.

JEFFREY FREDMAN
PRIMARY EXAMINER
4/11/05

Continuation of 11. does NOT place the application in condition for allowance because: Applicants' arguments are fully reviewed and found not persuasive for the reasons that follow. On page 7, paragraph 1, of the response, Applicants argue that the assertion made by the examiner that an amino acid change in the NE transporter (NET) gene product that results in sub-optimal NE transport in one group of patients would not be expected to result in sub-optimal NE transport in another group of patients has no scientific basis, and assert that a mutation in NET gene would be predicted to function in OI patients and non-OI patients similarly with respect to NE transport. Applicants' arguments are fully considered and found unpersuasive because every mutation has a specific function and the generalized statement that a mutaion in NET would be predicted to function in OI patients and non-OI patients similarly with respect to NE transport is not persuasive. The existance of the specific NET mutation (A457P) in OI patients and non-OI patients can be predicted to work similarly in both the groups, but not all other mutations in NET transporter gene would have the same or similar effect as A457P mutation. Thus the instant specification fails to enable that any mutation in NET gene would have the similar effect, that is, result in sub-optimal NE trnasport. The instant specification only enables a speicfic mutaiton (A457P) in OI patients with a sub-optimal NE transport and does not enable for any other mutation in NET having similar effect on NE transport.

On page 7, paragraph 2, of the response Applicants further argue that the method steps drawn to screening for suceptibility of a NET gene encoding an amino acid change and detecting patiens with OI is enabled. Applicants' arguments are fully considered and found unpersuasive because the instant specification enables only one specific mutation that encodes an amino acid change at a location and is correlated to OI. The specification fails to enable correlation of any other mutation in NET gene with an amino acid change and fails to correlated any other mutation in NET gene with OI. The method is not directed to that specific (A457P) mutation, rather broadly is drawn to any mutation that encodes an amino acid change, which is not supported by the instant specification. Thus Applicants' assertions that no scientific basis for the distinction between subjects with OI and subjects in general is unpersuasive because the distinction was made between a specifc mutation vs any mutation in NET and not between OI patients with the said speicfic mutation and subjects in general having that specific mutation. Claiming all mutations of NET gene (known and unknown) that encode an amino acid change is not enabled by the instant specification.

On page 8-9 of the response, Applicants further argue that the instant specification provided examples directed to the use of SEQ ID NO. 1 and 2 and invitro assays in chinese hamster ovary using the specific A475P polymorphism and argue that one of ordinary skill in the art would recognize that the specific polymorphism would be adopted for testing any nucleic acid sequence encoding a polymorphic NET polypeptide and also assert that these specific examples were not addressed by the examiner in the earlier response. Applicants' assertions are fully reviewed and Examiner notes that the assertions were indeed addressed by the Examiner on page 7, paragraphs 1-2 of the previous office action. In resopse to these assertions Examiner reiterates that the specific examples and pharmiocological testing would certainly be recognized by one of the ordinary skill in the art to adapt similar testing to explore new mutaitons in NET gene, however, the specification does not provide any support for such testing would result in mutations with altered amino acid change correlated to sub-optimal NE transport other than A457P mutation . Thus the specification fails to provide that any mutation in NET gene would lead to an amino acid change and lead to a sub-optimal NE transport..

Applicants' assertions on page 10 of the response that any subject carrying the A457P mutation would be expected to suffer sub-optimal NE transport regardless of whether or not they had OI, is fully considered. Examiner agrees that the specifc mutation (A457P) is responsible for sub-optimal NE transport in any subject having this specific mutation, for which the specification has porvided support. However, the instant specification lacks support for any correlation between any other mutation in NET gene and sub-optimal NE transport.. Further one skill in the art would predict that subjects having this specific mutation would be expected to develop OI. Examiner notes that Applicants' assertions on page 10 directed to misinterpretation of examiner's response to a distiction between the OI and non-OI patients, infact Examiner made it clear that the specification lacks support for correlation between any mutation other than A457P in NET gene and sub-optiaml NE transport .

On page 10-11 of the reponse Applicants argue that the claims are drawn to a method for detecting a polymorphism of NET gene encoding an amino acid change , so as to eliminate mutations that do not alter the polypeptide sequence, and further argue that the identification of the A457P polymorphism with sub-optimal transport in OI patients provides a connection between a polymorphism in NET and a sub-optimal NE transport phenotype and the invitro assays using CHO confirm the characterization of sub-optimal activity with the A457P mutation. Applicants also argue that the subsequent work by others, identified several additional mutations their association with an amino acid change and sub-optiaml NE transport phenotype. Applicants' arguements are fully reviewed and found not persuasive. At the time the invention was made only A457P mutation was identified and correlated with sub-optimal NE transport phenotype. Thus the specification has enabled a specific mutation and its correlation to sub-optimal NE transport phenotype and the instant specification, at the time the invention was made does not enable a correlation between any mutation in NET in general and sub-optimal NE transport. Thus the rejection under 35 USC, 112, first paragraph is maintained herein and the newly added claim 80 herewith rejected under 35 USC 112, first paragraph since claim 80 falls with in the scope of this rejection.